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REMARKS/ARGUMENTS

With this amendment, claims 1-28 are pending. Claims 2-8 are withdrawn. Claims 9 and 25 are cancelled without prejudice. New claim 29 is added. For convenience, the Examiner's rejections are addressed in the order presented in a July 7, 2006, Office Action.

I. Status of the claims

Claim 1 is amended to recite a pharmaceutical composition comprising an ADNF III polypeptide comprising the active core site of SEQ ID NO:2. Claim 1 is also amended to recite prevention or treatment of multiple sclerosis. Support for these amendments is found throughout the specification, for example, at original claim 1, pages 16-22, and at page 22, line 4 through page 24, line 10 and at page 30, line 1 through page 31, line 11. Claim 11-17, 23, 24, and 26-28 are amended to correct dependency. Claims 15 and 22 are amended to correct alleged grammatical errors. New claim 29 is added and recites that "proliferation of an immune cell in the subject is inhibited." Support for this amendment is found throughout the specification, for example, at page 31, lines 5-11. Claims 9 and 25 are cancelled without prejudice to subsequent revival. These amendments add no new matter.

II. Objections to the specification

The first paragraph of the specification is updated to reflect the current status of all priority documents. Paragraph 02 of the specification has not been modified. The Office Action fails to provide any legal justification for the removal of the paragraph and Applicants are not precluded from incorporating by reference the patents and patent applications listed in paragraph 02.

III. Incorporation by reference

The Office Action alleges that Applicants are required to amend the specification to provide specific ADNF III sequences. This requirement apparently originates with the Office Action's interpretation of the written description and enablement requirements under 35 U.S.C.

§112, first paragraph. Applicant's decline to amend the specification as suggested in the Office Action largely because the Office Action's application of the written description and enablement requirements to nucleotide and amino acid sequences is incorrect. Under recent decisions from Federal Circuit Court of Appeals, the disclosure of the specification, in fact, exceeds the written description and enablement requirements for nucleotide and amino acid sequences. Complete arguments regarding the written description and enablement requirements are below.

IV. Objections to the claims

Claims 1, 14, and 17-22 are objected to for allegedly containing subject matter directed to a non-elected invention. Claim 1 is amended and now recites ADNF III polypeptides. The Office Action recognizes that claim 1 is a generic claim. *See, e.g.*, Office Action rejections for alleged lack of enablement and written description. Claim 14 is directed to peptides that comprise the elected ADNF III active core sequence. To the extent that claim 14 may include non-elected subject matter, Applicants respectfully assert that, after choosing SEQ ID NO:2 as the elected species of generic claim 1, Applicants are entitled to maintain claims directed to non-elected species. "Upon allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable claim as provided by 37 C.F.R. 1.141." MPEP809.02(a). With regard to claims 17-22, these claims depend from generic claim 1 and include additional components in the ADNF III pharmaceutical composition. Again, Applicants assert their right to maintain claims directed to any allegedly non-elected subject matter.

Claims 15 and 22 are objected to for an alleged typographical error. Although Applicants believe that claims 15 and 22 are clear as originally drafted, claims 15 and 22 are amended to expedite prosecution.

Claim 25 is objected to because of certain informalities. In order to expedite prosecution, claim 25 is now cancelled.

V. Rejections under 35 U.S.C. §112, first paragraph, enablement

Claims 1 and 9-28 are rejected under 35 U.S.C. §112 first paragraph, because the specification allegedly does not enable the full scope of the claims. To the extent the rejection applies to the amended claims, Applicants respectfully traverse the rejection. The Office Action alleges that the specification does not enable treatment of all autoimmune diseases using the claimed methods. In order to expedite prosecution, claim 1 is now amended to recite treatment and prevention of multiple sclerosis.

With regard to the sequence of full length ADNF III, the Examiner appears to have focused improperly on inoperative embodiments, leading to the conclusion that undue experimentation would be required to use the claimed methods. However, the proper test of enablement is "whether one skilled in the art could make or use the claimed invention from the disclosure in the patent coupled with information known in the art without undue experimentation" (*see, e.g.*, MPEP §2164.01). In the present application, one of skill would know how to avoid inoperative embodiments without undue experimentation (*see, In re Cook and Merigold*, 169 USPQ 299, 301 (C.C.P.A. 1971)). Moreover, the present application provides guidance in the form of assays and working examples for treatment of an autoimmune disorder at page 22, line 4 through page 24, line 10 and at page 30, line 1 through page 31, line 11.

Claims reading on inoperative embodiments are enabled if the skilled artisan understands how to avoid inoperative embodiments. As described by the court in *In re Cook and Merigold*, 169 USPQ 302:

> Many patented claims read on vast numbers of inoperative embodiments in the trivial sense that they can and do omit 'factors which must be presumed to be within the level of ordinary skill in the art'....There is nothing wrong with this so long as it would be obvious to one of ordinary skill in the relevant art how to include those factors in such a manner as to make the embodiment operative rather than inoperative.

See, In re Cook and Merigold, 169 USPQ at 302 (quoting in part *In re Skrivan*, 166 USPQ 85, 88 (C.C.P.A. 1970)).

Factors such as the amount of guidance presented in the specification and the presence of working examples must be considered to determine whether undue experimentation is required to practice the claimed invention (*see, Ex Parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Int. 1985) and *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988)). As described in *Wands*, "a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed" (*see, Wands*, USPQ2d at 1404, quoting *In re Jackson*, 217 USPQ 804 (Bd. Pat. App. & Int. 1982)).

The specification provides standard assays and working examples for treatment and prevention of multiple sclerosis as well as the minimum, core ADNF III sequence required for a beneficial effect. (*See, e.g.*, specification at page 22, line 4 through page 24, line 10 and at page 30, line 1 through page 31, line 11.) Those of skill in the art would clearly be able to use the specification to identify appropriate patients and practice the methods of the invention for treatment and prevention of multiple sclerosis. Identification of operable embodiments, therefore, is well within the means of one of skill of the art, without undue experimentation.

Moreover, "[a] patent need not teach, and preferably omits, what is well known in the art." MPEP 2164.01 *citing In re Buchner*, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991); *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 231 USPQ 81, 94 (Fed. Cir. 1986), *cert. denied*, 480 U.S. 947 (1987); *Lindemann Maschinenfabrik GMBH v. American Hoist & Derrick Co.*, 221 USPQ 481, 489 (Fed. Cir. 1984). As discussed below, therefore, the rejections for alleged lack of enablement of full length ADNF III polypeptides should be withdrawn.

The Federal Circuit has recently issued an opinion on the amount and type of disclosure required to enable an amino acid or nucleic acid sequence recited in a claim. The court ruled that where sequences had been disclosed previously in professional journals and were, thus, readily accessible to the public, enablement did not require incorporation by reference, much less recitation of the actual sequences in the application. *See, e.g., Falkner v. Inglis*, 79 USPQ2d 1001, 1006 (Fed. Cir. 2006). Here, the Office Action has cited sequences of full length ADNF III polypeptides, and each sequence was publicly available before the filing date of the present application. The Office Action goes on to assert that the sequences must be

added to the specification to provide enablement of the claims. However, recitation of known sequences is **not** required to meet the enablement standard put forth by the Federal Circuit and thus, this rejection should be withdrawn.

The Office Action also alleges that the specification does not provide enablement for prevention of an autoimmune disease. This is incorrect. The specification discloses genetic tests to identify patients that are candidates for multiple sclerosis at page 23, lines 20-27. The specification also discloses tests to determine the efficacy of prevention at page 23, line 28 through page 24, line 10. Thus, the specification enables claims to prevention of multiple sclerosis.

In view of the above amendments and arguments, withdrawal of the rejection for alleged lack of enablement is respectfully requested.

VI. Rejections under 35 U.S.C. §112, first paragraph, written description

Claims 1 and 9-28 are rejected under 35 U.S.C. §112, first paragraph for allegedly failing to comply with the written description requirement. According to the Office Action, the specification does not provide adequate description of the genus of ADNF III polypeptides that comprise SEQ ID NO:2. The Office Action alleges that those of skill would not recognize that the inventors had possession of the claimed invention at the time of filing and objects specifically to the description of full length ADNF III polypeptides. In response, Applicants respectfully traverse the rejection.

As US patent law is currently applied, the specification does describe the distinguishing characteristics of a genus of ADNF III amino acid sequences. The Federal Circuit court of Appeals addressed the description adequate to show one of skill that the inventors were in possession of a claimed genus at the time of filing. *See, e.g., Enzo Biochem, Inc. v. Gen-Probe, Inc.*, 63 USPQ2d 1609 (Fed. Cir. 2002). An applicant may also show that an invention is complete by

> . . . disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that applicant was in possession of the claimed invention . . . *i.e.*, complete or partial structure, other physical and/or chemical properties,

> functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. *Id.* at 1613.

Furthermore, "description of a representative number of species does not require the description to be of such specificity that it would provide individual support for each species that the genus embraces." *See, e.g.*, 66 Fed. Reg. 1099, 1106 (2001).

Here the specification provides the structure of the ADNF III core sequence, *i.e.*, SEQ ID NO:2, and the correlating function, *i.e.*, treatment of multiple sclerosis. The claimed genus is the group of polypeptides that comprise SEQ ID NO:2 and have the disclosed function. Functional assays and experimental data are disclosed in the specification, *e.g.*, at page 22, line 4 through page 24, line 10 and at page 30, line 1 through page 31, line 11. As the specification discloses the polypeptide structure and experimental data to support the claimed function, those of skill would understand that the inventors had possession of the claimed invention at the time of filing.

The Office Action again cites known ADNF III sequences and alleges that such sequences must be recited in the specification or sequence listing to provide description of the claimed genus. This position is inconsistent with recent decisions by the Federal Circuit Court of Appeals. First, the Federal Circuit has made it clear that there is no per se rule regarding inclusion of sequence information in a patent application to support description of a nucleic acid sequence, and by analogy an amino acid sequence. "When the prior art includes the nucleotide information, precedent does not set a per se rule that the information must be determined afresh." *Capon v. Eshar*, 76 USPQ2d 1078, 1084-5 (Fed. Cir. 2005). In fact, the Federal Circuit has recently ruled that even incorporation by reference of known sequences is not required for the written description requirement. "Accordingly we hold that where, as in this case, accessible literature sources clearly provided, as of the relevant date, genes and their nucleotide sequences. . . , satisfaction of the written description requirement does not require either the recitation or incorporation by reference (where permitted)of such genes and sequences." *Falkner v. Inglis*, 79 USPQ2d 1001, 1008 (Fed. Cir. 2006). Thus, the genus of ADNF III polypeptides used in the

claimed methods is adequately described. More disclosure is not required to demonstrate that the inventor's had possession of the genus at the time of filing.

In view of the above amendments and arguments, withdrawal of the rejection for alleged lack of written description is respectfully requested.

VII. Rejections under 35 U.S.C. §112, second paragraph

According to the Office Action, claims 1 and 9-28 are indefinite for allegedly failing to include a correlation step. In order to expedite prosecution, claim 1 is now amended to recite "thereby treating or preventing multiple sclerosis in the subject." According to the Office Action, claims 15 and 22 are indefinite for inclusion of functional or operational language. In order to expedite prosecution, claims 15 and 22 are now amended.

In view of the above amendments and arguments, withdrawal of the rejection for alleged indefiniteness is respectfully requested.

VIII. Rejections under 35 U.S.C. §102

Claims 1, 9-11, 14-15, 17, and 20-28 are rejected as allegedly anticipated by either WO 98/35042 or by US Patent No. 6,613,740 (Gozes *et al.*). To the extent the rejections apply to the amended claims, Applicants respectfully traverse the rejections.

To anticipate a claim, the reference must teach every element of the claim. "A claim is anticipated only if each and every element as set forth in the claim is found...in a single prior art reference." *Verdegaal Bros. v. Union Oil of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). Thus, in order to anticipate, the cited references must contain every element of the claims at issue. The cited references do not.

A. WO 98/35042

According to the Office Action WO 98/35042 discloses treatment of Guillian-Barre Syndrome and therefore allegedly anticipates the claims. In order to expedite prosecution, claim 1 is now amended to recite preventing or treating multiple sclerosis by administration of a pharmaceutical composition that comprises an ADNF III polypeptide.

WO 98/35042 discloses treatment of a number of diseases using an ADNF III polypeptide. WO 98/35042 does not specifically disclose treatment or prevention of multiple sclerosis using an ADNF III polypeptide. Therefore, WO 98/35042 does not disclose all the elements of the amended claims and cannot anticipate the claims.

B. Gozes et al.

According to the Office Action Gozes *et al.* discloses treatment of Guillian-Barre Syndrome and therefore allegedly anticipates the claims. In order to expedite prosecution, claim 1 is now amended to recite preventing or treating multiple sclerosis by administration of a pharmaceutical composition that comprises an ADNF III polypeptide.

Gozes *et al.* discloses treatment of a number of diseases using an ADNF III polypeptide. Gozes *et al.* does not specifically disclose treatment or prevention of multiple sclerosis using an ADNF III polypeptide. Therefore, Gozes *et al.* does not disclose all the elements of the amended claims and cannot anticipate the claims.

In view of the above amendments and remarks, withdrawal of the rejections for alleged anticipation is respectfully requested.

IX. Rejections under 35 U.S.C. §103(a)

Claims 1, 9-15, and 17-28 are rejected as allegedly obvious by either WO 98/35042 or by US Patent No. 6,613,740 (Gozes *et al.*) in view of either US2002/001301 (Brenneman *et al.*) or Voet *et al.* and Goodman *et al.* To the extent the rejections apply to the amended claims, Applicants respectfully traverse the rejections.

To establish a *prima facie* case of obviousness, three basic criteria must be met: (1) there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings; (2) there must be a reasonable expectation of success; and (3) the prior art reference must teach or suggest all the claims limitations. MPEP§2143. See also *In re Rouffet*, 47 USPQ2d 1453. The court in *Rouffet* stated that "even when the level of skill in the art is high, the Board must identify specifically the principle, known to one of ordinary skill, that

suggests the claimed combination." *Rouffet* at 1459. The court has also stated that actual evidence of a suggestion, or teaching, or motivation to combine is required and the showing of a suggestion, or teaching, or motivation to combine must be "clear and particular." *In re Dembiczak*, 50 USPQ2d 1614, 1617 (1999). Under the standards listed above, the Office Action does not establish a prima facie case of obviousness.

A. WO 98/35042 or Gozes et al. in view of Brenneman et al.

Claims 1, 9-11, 14-17, and 20-28 are rejected under 35 U.S.C. §103(a) WO 98/35042 or Gozes *et al.* in view of Brenneman *et al.* According to the Office Action both Gozes *et al.* and WO 98/35042 teach methods of using ADNF III polypeptides for treatment an prevention of neurological difficulties; Brenneman *et al.* allegedly teaches administration of ADNF polypeptides or nucleic acids by recited means to treat conditions related to increased neuronal cell death. According to the Office Action, based on the teachings of the cited references, those of skill would have reasonably expected success in treating an autoimmune disease using an ADNF III polypeptide. Applicants respectfully disagree.

The arguments presented by the Office Action appear to assert that the claimed species of diseases treated with ADNF III polypeptides are part of a genus of treatable diseases listed in the cited references. However, none of the cited references, Gozes *et al.*, WO 98/35042, or Brenneman *et al.* specifically call out the claimed species, *i.e.*, treatment of multiple sclerosis. The Office Action fails to demonstrate that one of skill would go beyond the listed diseases to arrive at multiple sclerosis.

Although the Office Action asserts that the combination of references renders the claimed invention obvious, the Office Action also asserts that the specification does not enable treatment of autoimmune diseases, apparently including multiple sclerosis. *See, e.g.*, Office Action at page 5-6. The enablement and obviousness arguments presented in the Office Action are incompatible and one or both should be withdrawn.

Finally, the cited references disclose and demonstrate prevention of neuronal cell death after administration of ADNF III proteins. Using a mouse model for multiple sclerosis, the specification provides evidence that administration of ADNF III protein inhibits proliferation of

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immune cells. *See. e.g.*, specification at page 31, lines 5-11 and new claim 29. The cited references provide no teachings that would lead those of skill to predict that administration of ADNF III would have an effect on immune cell proliferation and thus would be useful to treat autoimmune disease, including multiple sclerosis.

B. WO 98/35042 or Gozes et al. in view of Voet et al. and Goodman et al.

Claims 1, 9-15, and 17-28 are rejected as allegedly obvious by either WO 98/35042 or by Gozes *et al.* in view of Voet *et al.* and Goodman *et al.* The alleged disclosures of WO 98/35042 and Gozes *et al.* are provided above. Voet *et al.* and Goodman *et al.* provide general teaching on the advantages of peptides comprising D-amino acids. Neither Voet *et al.* nor Goodman *et al.* provide any teachings regarding treatment of disease using ADNF III polypeptides. Thus, Voet *et al.* and Goodman *et al.* cannot overcome the deficiencies of WO 98/35042 or Gozes *et al.* listed above. The citation of WO 98/35042 or by Gozes *et al.* in view of Voet *et al.* and Goodman *et al.* is also inconsistent with the arguments raised against enablement of the claims. This group of cited references also fails to render predictable inhibition of immune cell proliferation by administration of ADNF III polypeptides.

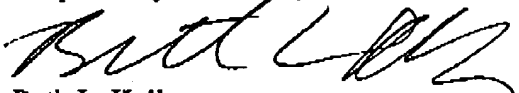
In view of the above amendments and remarks, withdrawal of the rejections for alleged obviousness is respectfully requested.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,



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